REMARKS

Claims 11-16 were pending. All pending claims were rejected in the Office Action. In view of the arguments that follow, Applicants respectfully request withdrawal of the rejection upon reconsideration.

Preliminarily, Applicants note with appreciation the withdrawal of all previous rejections.

Rejection under 35 U.S.C. § 103(a)

Claims 11-16 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zapata[a] et al. (FASEB J. 1995. 9:A1479) in view of Griffiths et al (U.S. Patent 5,670,132, filed 09/20/1994. Applicants traverse this rejection.

The Office argues that Zapata[a] et al. teach a Fab' fragment which contains a single cysteine in the hinge region including coupling of monomethoxypoly(ethylene glycol) to the cysteine. The Office admits that Zapata[a] et al. does not, however, teach a polymer of 25,000 to about 40,000 Da, or a composition with a carrier or fragment with an effector or reporter molecule. The Office alleges that these deficiencies are made up for by the teachings of Griffith et al.

Preliminarily, Applicants maintain that there is no motivation to modify Zapata[a] et al. to derive Applicants' invention. Zapata[a] et al. states that the 10kDa-MePEG-Fab' had a permanence time extended beyond that of the $F(ab')_2$ molecule, and did not affect the binding of antigen. Nonetheless, Applicants will address the Office's arguments.

The Office alleges that Griffiths et al. teaches site specific conjugation of PEG to Fab or Fab' outside the variable region, wherein the molecular weight of the PEG can be 30,000 Da and, also, an antibody conjugated to 1-10 PEG moieties of 5,000 Da, to reduce renal uptake and retention of the PEGylated antibody fragment after radiolabelling. Griffiths et al., however, does not describe a PEG of 30,000 Da. It provides a range of suitable PEGs having molecular weights of 1,000-30,000 (col. 3, lines 12-15). The disclosure of a range is not a disclosure of the endpoints of the range. *Atofina v. Great Lakes Chemical Corp.*, 78 USPQ2d 1417, 1424 (Fed. Cir. 2006). The Office also alleges that Griffiths et al. teaches site specific conjugation of PEG to an Fab or Fab' where the molecular weight can be 5000 Da to 50,000 Da. As acknowledged by the Office, however, Griffiths et al. discusses using 1-10 PEG-5,000 moieties. The Office has incorrectly interpreted this discussion to be a disclosure

of attaching a **single** PEG moiety of 5,000 Da to 50,000 Da. The Office's interpretation is patently incorrect. Thus, Applicants submit that Griffiths et al. does not teach a polymer of molecular weight 25,000 to 40,000 Da and, accordingly, even if combined, Zapata[a] et al. and Griffiths et al. do not result in Applicants' invention.

Further, Griffiths et al. actually teaches away from Applicants' invention. Although the Office acknowledges that the antibody fragments of Griffiths et al. are radiolabelled, it ignores this aspect in its analysis. This oversight is significant.

Griffiths et al. discusses producing free thiol groups for direct labeling with the radiolabel, i.e., Tc-99m. Griffiths et al. further discusses that the disulphide bonds in the hinge region of the antibody are generally more accessible to reducing agents and can be selectively cleaved. Griffiths et al. further notes that reducing the disulphide bonds that link light and heavy chains is not desirable. See Griffiths et al., column 4, line 47, through column 5, line 3. Griffiths et al., thus, specifically describes attaching the radiolabel to a *hinge region* thiol, i.e., cysteine.

Applicants' claims recite that the fragment comprises a hinge region with a **single** cysteine, to which the polymer, e.g., PEG, is attached. Griffiths et al. teaches that the radiolabel is to be attached to a hinge region cysteine. Thus, if a single cysteine is present in the hinge region of the fragment, it is to be radiolabelled, not pegylated, according to Griffiths et al. The Office cannot simply ignore this aspect of Griffiths et al.

> A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

MPEP 2141.02, emphasis in the original. Griffiths et al., thus, teaches away from a fragment having a single hinge region cysteine to which a polymer is attached

Applicants request that this rejection be withdrawn.

CONCLUSION

Applicants submit that all claims are in condition for allowance, and respectfully requests early notification of the same. If the Examiner disagrees, he is requested to contact the undersigned at the number provided below.

Respectfully submitted,

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